REMARKS

Claims 17, 20, 21 and 40-43 presently appear in this case. No claims have been allowed. The official action of March 8, 2006, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to an RNA molecule that targets mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:10. The targeting preferably prevents processing, splicing, transport, or translation of the mRNA, or results in mRNA degradation. The RNA may be an antisense RNA or a ribozyme.

The examiner has objected to the amendment filed December 15, 2005, under 35 U.S.C. §132(a) because it allegedly introduces new matter into the disclosure. The examiner refers to the amendments to paragraphs [0056] and [0059]. The examiner states that the Holzmayer and Whitesell references are disclosed in the instant specification as general references, but the disclosures of antisense RNA therein are not specifically pointed to or specifically contemplated in the context of the invention as it is now claimed. The examiner has required applicant to cancel the new matter in reply to this Office action. The examiner also discusses the new matter issue in the context of a 35 U.S.C. §112 rejection. The examiner stated there that the required

description of antisense oligonucleotides that are RNA antisense oligonucleotides is considered to be essential matter and cannot be incorporated by reference from applicants' cited references. This rejection is respectfully traversed.

The examiner is absolutely correct that essential subject matter cannot be incorporated by reference to a publication. However, such an improper incorporation by reference can be cured by amending the specification to physically insert the subject matter that had previously appeared only in the publication. See 37 C.F.R. §1.57(g). Improper incorporation by reference of essential material can be corrected. The examiner's attention is invited to MPEP §608.01(p), particularly section A.2., where it states:

> An incorporation by reference of essential material to an unpublished U.S. patent application, a foreign application or patent, or to a publication is improper under 37 CFR 1.57(c). The improper incorporation by reference is not effective to incorporate the material unless corrected by the applicant (37 CFR 1.57(g)). Any underlying objection or rejection (e.g., under 35 U.S.C. 112) should be made by the examiner <u>until applicant corrects the improper incorporation by reference by submitting an amendment to amend the specification or drawings to include the material incorporated by reference</u>. A statement that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter is also required. [Emphasis added]

See also Form Paragraph 6.19 quoted in this same section of the MPEP, which specifically instructs an applicant that an improper incorporation of essential material in the specification by reference to a publication may be corrected by amending the disclosure to include the material incorporated by reference. This is exactly what applicants did in the amendment of December 15, 2005.

The insertions are not new matter if they were previously incorporated by reference. In paragraph [0164], all of these references were specifically incorporated by reference "in order to more fully describe the state of the art to which this invention pertains."

The portion of the present specification directed to antagonists of a protein having a sequence as set forth in SEQ ID NO:10 begins at paragraph [0055]. The protein having the sequence as set forth in SEQ ID NO:10 is a novel protein, and the gene encoding it is a novel gene. The novelty of the present invention resides in the novelty of these new proteins and genes. Antisense antagonists are well known in the art. While the present claims are drawn to such mRNA antagonists, the novelty does not lie in the concept of an antagonist, which is well known in the art. The novelty lies in the specific mRNA that is being targeted by the antagonist. In paragraph [0056], many reviews are disclosed covering the main

aspects of antisense technology. That paragraph refers to "AS nucleotide sequences." The term "AS nucleotide sequences" is broad enough to read on the previously known DNA antisense sequences and the previously known RNA antisense sequences. The present specification as filed explicitly acknowledges that such RNA sequences were known, as can be seen from the titles explicitly spelled out on page 80 for the Holzmayer 1992 publication and page 87 for the Whitesell publication. These titles specifically refer to the well-known RNA antisense nucleotide sequences.

The examiner points out that in paragraph [0057] the specification states, "AS oligonucleotide sequences may be short sequences of DNA ...." However, the term "may be" is clearly not limiting, and this is but one example of an AS nucleotide sequence, as is the reference to "interaction of AS with genomic DNA to form a triple helix" later in the same paragraph. This is simply another example of AS oligonucleotides. No one reading the specification as a whole would interpret these examples as being exclusive. Furthermore, the reference to uracil as one of the possible bases of the oligonucleotides defined in the specification as set forth in paragraph [0064], makes clear that the term "oligonucleotide" as used throughout the specification is intended to encompass RNA.

Accordingly, the list of references at the end of the specification, all of which were incorporated by reference into the specification, clearly shows on its face that RNA antisense molecules were known in the prior art as examples of AS oligonucleotides. Indeed, the concept of the antisense molecule being an RNA molecule appears in the specification even without incorporation of anything by reference as the titles of those specific references were explicitly set forth in the specification as filed, not merely incorporated by reference. Thus, the amendment to paragraph [0056] need not be considered as an amendment that physically inserts that which had previously been incorporated by reference. It can simply be seen as inserting in paragraph [0056] the exact same information that was present in the application as filed on page 80. The same is true with the insertion to paragraph [0059] and the original disclosure on page 87.

Accordingly, whether these insertions are considered to be amendments of the specification to physically insert subject matter that had previously been incorporated by reference, or they are merely considered to be moving to one part of the specification information that was clearly set forth in another part of the specification, is irrelevant because in either event the insertions are not new matter. They merely recognize that antisense mRNA was disclosed in the

specification as being part of the prior art, thus providing support for the concept that the term "antisense oligonucleotide" includes antisense RNA. It is this fuller description of the prior art that has been incorporated by reference into the specification that supports the amendments made to the specification that make explicit that antisense RNA is part of the known aspects of antisense technology, and would be considered by those of ordinary skill in the art as being included in the term "AS nucleotide sequences" as used in the specification. Accordingly, reconsideration and withdrawal of this objection are respectfully urged.

The examiner has reviewed the claims and opined that the effective filing date of claims 17-19 and 21-23 is considered to be August 21, 1998, and the effective filing date of claims 20 and 22 is considered to be March 6, 2002. However, as this determination is not relevant to any of the present rejections, it is not necessary to respond to it. It should be explicitly understood, however, that failure to rebut these opinions of the examiner at this time is without prejudice, and no concession as to the examiner's opinions or agreement therewith can be implied by the present response.

Claims 20 and 22 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written

description requirement on the basis that they are directed to new matter. This rejection is respectfully traversed.

Claims 22 has now been deleted and support for claim 20 is found in paragraph [0056], particularly as amended. Even without the amended portion of the specfication, the sentence in paragraph [0056] at page 22, lines 9-14, that ample information has accumulated about the *in vitro* use of AS nucleotide sequences, coupled with the publication titles set forth at page 76-87 of the present specification, and particularly the titles of the Holzmayer and Whitesell publications within the list, establishes that antisense RNA is part of the accumulation of ample information. This clearly establishes that the description allows persons of skill in the art to recognize that the inventors invented what is claimed, i.e., the inventors were in possession of the concept of antisense oligonucleotides that are RNA molecules. Thus, claim 20 is supported by an adequate written description. See MPEP §2163.02. Furthermore, the discussion hereinabove with respect to the new matter objection to the specification is hereby incorporated by reference. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 17-23 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written

description requirement. The examiner states that claims drawn to RNA molecules that target an mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:10 reads on a large genus of RNA molecules that "target" the mRNA, which can have a large number of nucleotide sequences due to codon degeneracy. This rejection is respectfully traversed.

The claims have now been amended so as to substantially narrow their scope. Claim 40 is directed to antisense RNA consisting of a sequence that is the complement of at least seven nucleotides of target mRNA encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO:10. This is very specific and does not include a large number of nucleotide sequences due to codon degeneracy. Claim 40 also includes sequences that are the complement of at least seven nucleotides of target mRNA encoding a polypeptide that is an analog of the sequence of SEQ ID NO:10, having at least 95% homology thereto. This language is supported by the present specification at paragraph [0036] on page 14 of the specification, which states that an "analogue" preferably has 95% homology to the nucleotide sequence of which it is an analog.

Claim 41 specifies an RNA molecule consisting of a sequence that is the complement of at least seven nucleotides

of target mRNA encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO:10 or an analog of such an RNA molecule having at least 95% homology thereto and substantially retaining the targeting function. This language is supported, for example, by the language in the last sentence of paragraph [0058] on page 25. This sentence indicates that the antisense oligonucleotides include analog substitutions that do not substantially affect function. The definition of analog substitution is as discussed above in paragraph [0036]. The function referred to in paragraph [0058] is clearly the targeting function in the context of claim 41. Accordingly, this language is also supported by the specification and permits only a small degree of breadth from the specific complement, requiring at least 95% homology in both cases. Claims 42 and 43 do not encompass analogs and certainly should not be considered broader than the written description.

Claim 17 is also restricted to 95% homology and thus should be considered free of the written description requirement, which is essentially a breadth rejection. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 17-23 remain rejected under 35 U.S.C. §102(e) or 35 U.S.C. §103(a) as being anticipated by or obvious over

Pavco for reasons previously set forth. This rejection is respectfully traversed.

First of all, Pavco discloses ribozymes. Claims 40-43 are directed to RNA antisense molecules and thus cannot be anticipated by Pavco. As to the ribozyme claims, the RNA molecule of Pavco does not consist of a sequence that is the complement of at least seven nucleotides of target mRNA, although it might comprise such a sequence. Furthermore, the examiner states that the Pavco sequence is at most 94% homologous and thus it falls outside the 95% homology restriction of all of the present claims. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 20 and 22 have been rejected under 35 U.S.C. §102(e) or 35 U.S.C. §102(a) as being anticipated or obvious over Monia. The examiner states that Monia discloses an antisense oligonucleotide that is 20 nucleotides in length and 80% complementary to an mRNA encoding a polypeptide of SEQ ID NO:10. This rejection is respectfully traversed.

As all of the present claims now require at least 95% homology, the present rejection is no longer applicable. Reconsideration and withdrawal thereof are respectfully urged.

Claims 20 and 22 have been rejected under 35 U.S.C. §102(b) or 35 U.S.C. §103(a), and claims 17-19, 21 and 23 have been rejected under 35 U.S.C. §102(e) or 35 U.S.C. §102(a) as

being anticipated by or obvious over Stinchcomb. The examiner states that Stinchcomb discloses as a binding site for a ribozyme that is 88% identical to instant SEQ ID NO:2. This rejection is respectfully traversed.

As discussed above, the present claims require at least 95% homology, thus this rejection has been obviated. Reconsideration and withdrawal thereof are respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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